CLAIMS

1. A method for the development of gene panels for diagnostic and therapeutic purposes, comprising the steps of:

a) isolating at least one biological sample from each of at least two groups of biological material containing mRNA and/or proteins;

b) analysing the expression level of at least one gene in at least one of the biological samples;

c) selecting the gene(s) exhibiting a different expression level between said at least two groups of biological material,

whereby a first knowledge base is generated;

d) analysing the level of cytosine methylation in the methylation relevant regions of at least one gene of at least one of the biological samples of step a), wherein the gene is selected on the basis of the first knowledge base;

e) selecting the gene(s) exhibiting a different level of cytosine methylation between said at least two groups of biological material,

whereby a second knowledge base is generated; and

f) adding selected genes from the second knowledge base to a gene panel.

2. Method according to claim 1, comprising that the biological material is isolated by means of a biopsy, by means of an operation on an individual, by means of a dissection, derived from a preserved biological sample, collected from body fluid(s) and/or collected directly from the environment.

3. Method according to claim 1 or 2, characterised in that the biological material comprises a eucaryotic and/or procaryotic cell line, a biopsy sample, blood, sputum, faeces, urine, cerebral liquid, tissue embedded in paraffin, tissue derived from eyes, intestine, brain, heart, prostata, kidney, lung, breast or liver, histological samples or a combination thereof.

4. Method according to any of claims 1 to 3, characterised in that at least one of the biological samples is derived from biological material of healthy and/or diseased individuals.

5. Method according to any of claims 1 to 4, characterised in that the isolation of said biological sample comprises isolating subcellular compartments, organelles, macromolecular structures and multiprotein complexes, partial or complete preparation of the mRNA, reverse transcription or partial digestion of the material with an enzyme selected from proteases, RNAses and/or DNAses or combinations thereof.

6. Method according to any of claims 1 to 5, characterised in that the analysis of the expression level of the at least one gene in the biological sample comprises determining the relative amount of mRNA or protein derived from said at least one gene.

7. Method according to claim 6, characterised in that the analysis comprises one- or two-dimensional gel electrophoresis, differential display, analysis of selected sets of tumour markers, subtractive hybridisation, mass spectrometry, comparative expressed sequence tag sequencing, representational difference analysis, cDNA or oligonucleotide arrays, serial analysis of gene expression, enzymatic, fluorescent, radioactive, dye and/or antibody labelling.

8. Method according to claim 7, characterised in that the analysis further comprises measuring intensities of expression during one- or two-dimensional gel electrophoresis, differential display, subtractive hybridisation, DNA, RNA or protein sequencing, mass spectrometry, and enzymatic, radioactive, dye and/or antibody labelling.

9. Method according to any of claims 6 to 8, characterised in that the analysis is at least partially performed by means of a suited automate, for example a robot.

10. Method according to any of claims 6 to 9, characterised in that the expression levels of at least two genes are analysed in parallel.

11. Method according claim 10, characterised in that the expression levels of at least 100 genes are analysed in parallel.

12. Method according to any of claims 1 to 11, characterised in that the selection is based on a combination of the analysis of both mRNA level and protein expression.

13. Method according to any of claims 1 to 12, characterised in that the selection is based on the result of at least two individual rows of analyses.

14. Method according to any of claims 1 to 13, characterised in that the selection is performed in such a way as to give a first knowledge base comprising only one set of selected genes.

15. Method according to any of claims 1 to 13, characterised in that the selection is performed in such a way as to give a first knowledge base comprising different subsets of selected genes.

16. Method according to any of claims 1 to 13, characterised in that the selection is at least partially performed automatically by means of a suited automate, such as a computer device.

17. Method according to any of claims 1 to 16, characterised in that at least two genes are selected in parallel.

18. Method according to claim 17, characterised in that at least 100 genes are selected in parallel.

19. Method according to any of claims 1 to 18, characterised in that the methylation relevant regions comprise the complete genes and/or promoters, introns, first exons and/or enhancers of the genes to be analysed.

20. Method according to any of claims 1 to 19, characterised in that the analysis of the level of cytosine methylation comprises chemical treatment with bisulphite, hydrogen sulphite or disulphite, polymerase chain reaction (PCR), hybridisation analyses, sequencing, mass spectrometry and fluorescent, enzymatic, radioactive, dye and/or antibody labelling.

21. Method according to any of claims 1 to 20, characterised in that the analysis is at least partially performed by means of a suited automate, for example a robot.

22. Method according to any of claims 1 to 21, characterised in that the level of cytosine methylation of at least two genes are analysed in parallel.

23. Method according claim 22, characterised in that the level of cytosine methylation of at least 100 genes are analysed in parallel.

24. Method according to any of claims 1 to 23, characterised in that the selection is based on the result of at least two individual rows of analyses.

25. Method according to any of claims 1 to 24, characterised in that the selection is performed in such a way as to give a second knowledge base comprising only one set of selected genes.

26. Method according to any of claims 1 to 25, characterised in that the selection is performed in such a way as to give a second knowledge base comprising different subsets of selected genes.

27. Method according to any of claims 1 to 26, characterised in that the selection is at least partially performed automatically by means of a suited automate, such as a computer device.

28. Method according to any of claims 1 to 27, characterised in that at least two genes are selected in parallel.

29. Method according to claim 28, characterised in that at least 100 genes are selected in parallel.

30. Method according to any of claims 1 to 29, characterised in that all or a part of the genes of the second knowledge base are added to the gene panel.

31. Method according to any of claims 1 to 30, characterised in that additional information about methylation relevant regions of the selected genes is added to the gene panel.

32. Method according to any of claims 1 to 31, characterised in that steps a) to f) are repeated.

33. Method according to claim 32, characterised in that it is repeated for at least 100 times.

34. Method according to any of claims 32 or 33, characterised in that the identical biological material, different biological material or a combination thereof is used in step a).

35. Method according to any of claims 1 to 34, characterised in that the steps are performed in the following order: step a), step d), step e), step b), step c), and step f).

36. Method according to any of claims 1 to 35, characterised in that it is at least partially performed by means of a suited automate, for example a robot.

37. Gene panel, obtainable according to a method according to any of claims 1 to 36.

38. Gene panel according to claim 37 comprising additional information data about methylation relevant regions of the selected genes, like the complete genes and/or promoters, introns, first exons and/or enhancers of the selected genes.

39. Gene panel according to claim 37 or 38 in the form of a knowledge base on a computer disc, RAM, ROM, or a printed table or listing.

40. Use of a gene panel according to any of claims 37 to 39 for the diagnosis of a disease.

41. Device for the generation of a gene panel according to any of claims 37 to 39, comprising
means for generating a first and second knowledge base according to claim 1; and
means for adding selected genes from the second knowledge base to a gene panel.

42. A method for the diagnosis of a disease, comprising the following steps:
a) providing a gene panel according to any of claims 37 to 39;
b) analysing the level of cytosine methylation at selected sites of the DNA based on said gene panel in biological material of at least one diseased individual with a known disease or medical condition and/or at least one healthy individual, thereby generating a first knowledge base;
c) analysing the level of cytosine methylation at selected sites of the DNA based on said gene panel in biological material of at least one diseased individual with an unknown disease or medical condition, thereby generating a second knowledge base; and
d) providing a third knowledge base comprising a plurality of expert rules for comparing the first and second knowledge base;
e) selecting a type of disease or medical condition for the at least one diseased individual with an unknown disease or medical condition based on said first to third knowledge bases.

44. Method according to claim 43, characterised in that the selected sites of the genes to be analysed are located in the promoters, introns, first exons and/or enhancers or combinations thereof.

45. Method according to claims 43 or 44, characterised in that the analysis of the level of cytosine methylation comprises chemical treatment with bisulphite, hydrogen sulphite or disulphite, polymerase chain reaction (PCR), hybridisation analyses, sequencing, mass spectrometry and fluorescent, enzymatic, radioactive, dye and/or antibody labelling.

46. Method according to any of claims 43 to 45, characterised in that the analysis is at least partially performed by means of a suited automate, for example a robot.

47. Method according to any of claims 43 to 46, characterised in that the level of cytosine methylation of at least two genes are analysed in parallel.

48. Method according claim 47, characterised in that the level of cytosine methylation of at least 100 genes are analysed in parallel.

49. Method according to any of claims 43 to 48, characterised in that steps b) to d) are repeated before performing step e).

50. Method according to claim 43 to 49, characterised in that it is repeated for at least 100 times.

51. Method according to any of claims 43 to 50, characterised in that the identical biological material, different biological material or a combination thereof is used in step c).

52. Method according to any of claims 43 to 51, characterised in that it is at least partially performed by means of a suited automate, for example a robot.

53. Use of a method according to any of claims 43 to 52 for the diagnosis of unwanted side effects of medicaments, cancers, dysfunctions, damages or diseases of the central nerval system (CNS), aggressive symptoms or behavioural disorders, clinical, psychological and social consequences of brain injuries, psychotic disorders and disorders of the personality, dementia and/or associates syndromes, cardiovascular diseases, malfunctions or damages, diseases, malfunctions or damages of the gastrointestine, diseases, malfunctions or damages of the respiratory system, injury, inflammation, infection, immunity and/or reconvalescence, diseases, malfunctions or damages as consequences of modifications in the developmental process,

diseases, malfunctions or damages of the skin, muscles, connective tissue or bones, endocrine or metabolic diseases, malfunctions or damages, headache, and sexual malfunctions or combinations thereof.

54. Use according to claim 53 for the diagnosis of leukemia, head and neck cancer, Hodgkin's disease, gastric cancer, prostate cancer, renal cancer, bladder cancer, breast cancer, Burkitt's lymphoma, Wilms tumor, Prader-Willi/Angelman syndrome, ICF syndrome, dermatofibroma, hypertension, pediatric neurobiological diseases, autism, ulcerative colitis, fragile X syndrome, and Huntington's disease.

55. Method for the treatment of a disease or medical condition, comprising
a) providing at least one diagnosis according to a method according to any of claims 43 to 52; and
b) installing a specific treatment for said at least one diagnosed disease or medical condition.

56. Method according to claim 55, wherein said specific treatment is disease specific and/or personalised.

57. Use of a method according to claims 55 or 56 or for the treatment of unwanted side effects of medicaments, cancers, dysfunctions, damages or diseases of the central nerval system (CNS), aggressive symptoms or behavioural disorders, clinical, psychological and social consequences of brain injuries, psychotic disorders and disorders of the personality, dementia and/or associates syndromes, cardiovascular diseases, malfunctions or damages, diseases, malfunctions or damages of the gastrointestine, diseases, malfunctions or damages of the respiratory system, injury, inflammation, infection, immunity and/or reconvalescence, diseases, malfunctions or damages as consequences of modifications in the developmental process,

diseases, malfunctions or damages of the skin, muscles, connective tissue or bones, endocrine or metabolic diseases, malfunctions or damages, headache, and sexual malfunctions or combinations thereof.

58. Use according to claim 57 for the treatment of leukemia, head and neck cancer, Hodgkin's disease, gastric cancer, prostate cancer, renal cancer, bladder cancer, breast cancer, Burkitt's lymphoma, Wilms tumor, Prader-Willi/Angelman syndrome, ICF syndrome, dermatofibroma, hypertension, pediatric neurobiological diseases, autism, ulcerative colitis, fragile X syndrome, and Huntington's disease.